tissue is already too extensive, that cannot be cured. Many cases, both in the first and second stages, can be cured by merely passing the summer out of doors in this country, but even in these, I believe wintering in Mexico would very much shorten the treatment. In all cases that have advanced to the third stage, wintering in Mexico should be recommended, as the treatment is much prolonged by the aggravation of the symptoms, during the time that the open air treatment has to be suspended. Every case, however, must be treated on its own merits; the time and means required for restoration to health, being more dependent on the general pathological and diathetic condition of the patient, than on the amount of change that has taken place in the lungs.

It is not my intention at present to enter on the questions of pathology and treatment which the above facts naturally suggest. This I hope to do on some future occasion. Their most important bearing I believe is, the support they bring to the views of those who place their chief reliance on the hygienic treatment of the disease. How striking a confirmation do these facts offer of the remark of Dr. Richardson, who, in his work on Consumption, observes:—

"In a cozy room the consumptive is bound never to live, nor in any room indeed, for any great length of time. So long as he is able to be out of doors, he is in his best and safest home. In the fields, on the hills, wherever the fresh air vivifies, where plants look most vigorous, and animals frisk about in the joy of health, there will the consumptive draw in his choicest medicine, there dissolve and throw off most freely the germs of his disease, and there repair most easily the tissues he has lost."—*The Hygienic Treatment of Pulmonary Consumption.* By Benjamin W. Richardson, M. D. Page 8.

ART. IV.—*On the Organic Nitrogenized Principles of the Body, with a New Method for their Estimation in the Blood.* By AUSTIN FLINT, JR., M. D., Professor of Physiology and Microscopy in the Bellevue Hospital Medical College, New York, and in the Long Island College Hospital.

PART I. *Composition and Properties of the Organic Nitrogenized Principles of the Body.*—The physiological investigator of the present day is greatly dependent upon Chemistry as a means of ascertaining the functions of the body; so much so, indeed, that these departments cannot be separated from each other, and it is to Physiological Chemistry we must look for the solution of questions of the highest importance which yet remain unanswered. Among the various questions which thus remain to be answered by the Chemist, that of the quantity, composition, condition of existence, and changes, of the organic nitrogenized principles is the most important; for these apparently are the constituents of the body endowed with vital properties; they regulate the changes which take place in the other principles, and the various modifications which they undergo in the body constitutes the mysterious "life," the comprehension of which has not yet been granted to the student of Nature. Though chemistry has enabled us to make but little, if any, progress towards the solution of the great question of vitality, it has helped us to comprehend certain of the phenomena of living bodies; and by long searching we have found out some of the laws which regulated their phenomena. The results of the physiological labours of centuries have only confirmed a great principle which must be recognized by every one who hopes to make any advance in this science.

The laws which regulate animated nature are irrevocably fixed; as distinct from those which govern inanimate objects as life is from death. They must be sought for by a patient study of the phenomena of life till the chain of evidence is complete. The mind must seek to comprehend, not to create.

Much ineffectual labour has resulted from a lack of comprehension of this great principle. While Physiology was comparatively new as a science, many endeavoured to establish laws for the regulation of the economy instead of adding to our knowledge of phenomena; and others, ignorant of the fact that what is true of inanimate matter cannot be applied to the living body, endeavoured to explain everything by physical or chemical laws. To this latter circumstance may be attributed the want of application of chemistry to physiology until within the last few years; though, in all ages, when learning has been cultivated, chemistry has been a favourite study. They who took such pride in the discovery of elements, and the establishment of physical laws, could not bring themselves to admit, and cannot, at the present day even, that the body is anything but a collection of those elements regulated by the laws with which they were familiar; while they who saw these laws so often violated in living bodies, were disposed to reject entirely chemical and physical explanations of physiological phenomena. Hence arose the classes of vital and chemical physiologists. To make use of chemistry, from which physiology had so much to expect, it was necessary to create a new mode of study which should have reference to organic substances, and to substances not necessarily chemical elements, but formed from these elements, which are now called *Proximate Principles.* It will be seen at once how important are these principles with reference to their condition and behaviour in the living body, and how necessary it is to study them from this point of view, and not simply as inorganic or inanimate compounds.

There is thus a manifest difference between a proximate principle and a chemical element. The former has certain properties in the living body which are different from any known in the inorganic world. They may be properties peculiar to animal substances, such as albumen or musculine, which are endowed in living bodies with the vital properties of continual destruction and reparation; or the substance may be inorganic, as water or chloride of sodium, but actually entering into the composition of organized tissues, and participating in the peculiar vital changes which they undergo. The latter is an indivisible substance, possessing no power of self-regeneration, forming definite compounds by unison with other elements of the same class, by which union the properties of all the components are radically changed. Chemical elements can be studied, and have been studied for years, without reference to organized or living structures, though these are formed necessarily of such elements, and as such have been found to possess certain definite properties. When the chemist, in investigating organic bodies, studies only the ultimate elements of which they are composed, he learns nothing more of the properties of these elements, for they are identical with those he extracts from inorganic substances. He gives us simply the results of decomposition of the body; while, what we wish to know, is, the function of the systems and organs, and the elements which compose the tissues of the body. The ultimate composition of organic bodies is manifestly of little importance compared with a knowledge of their physiological properties; unless, indeed, this should explain their function, a hope of the chemist which is rarely realized. Thus the body cannot advantageously be studied from a purely chemical point of view; and the changes which take place, even in its inorganic constituents, cannot be explained by formulæ which indicate simply the addition or subtraction of certain elements. Within a few years a great advance has been made in physiological chemistry by a modification of the mode of study of organic principles. The most rational investigators of the present day treat them as compound substances, which cannot be decomposed without destroying their properties. But a still further advance is necessary: they must be considered, not merely as proximate principles, which can be separated from the body by means which do not interfere with their chemical composition, but as principles capable of performing their functions only when united together, as they certainly are in Nature. For example, what has been considered as albumen, that is, dried albumen, is incapable of performing its function if it be not united with water, chloride of sodium, and other inorganic substances which are always found in connection with it; and though it be interesting to know its ultimate composition, and its behaviour on the application of heat, in the presence of acids, etc. etc., these phenomena are artificial, and useful only as tests; while our true line of inquiry lies in a study of its behaviour in the body, and the investigation of natural, rather than artificial phenomena. Instead of attempting to isolate it completely, we should rather study its union with the other principles by which it is enabled to perform its functions; and when we separate it from the animal fluids in order to ascertain its proportionate quantity, we should separate with it those other substances which are united with it in the living body, without which it can perform no vital functions. We shall see that some of these substances, as water, actually enter into the composition of the organic principles, and cannot be separated without alteration and decomposition.

These preliminary remarks explain why I consider it of the greatest importance to study, first of all, *the condition under which organic substances exist in the body;* more especially as this question is almost ignored by physiologists. We shall find that, to correspond with the ideas I shall present upon this important question, a new method of estimating the quantity of these substances will be necessary, as the analyses which we now have are the work of chemists who have not appreciated their condition of existence. In discussing this question, it will be necessary to review to some extent the opinions and analyses of chemists which are accepted at the present time.

Ultimate Composition of Organic Nitrogenized Substances.—According to the present received views, every tissue of the body, and all the fluids, with the exception of the excrementitious fluids, contain a characteristic element, which is found in no other situation, and which gives to it certain properties connected with nutrition, which may be called vital. Generally, these tissues and organized fluids contain but one characteristic organic element, which takes its name, with the termination *ine*, from the situation in which it is found. Thus *musculine* is the organic element characteristic of muscular tissue; *osteine*, of bony tissue; *cartilagine*, of cartilage: and among the fluids we have *pancreatine* for the pancreatic juice; *mucosine* for the mucus. With the exceptions of the blood and milk, there is but one such element to each tissue or fluid. The blood, however, which furnishes the material for the formation of all these substances, contains several organic substances, *i. e.*, *fibrin*, *albumen*,[1] and globuline; and the milk contains, in addition to *caseine*, a trace of albumen. Though it is probable that all the tissues and organized fluids (excrementitious fluids excepted) contain elements of this kind which are characteristic and present shades of difference for each one, they have not yet all been separated sufficiently for purposes of study; and, according to Robin and Verdeil, only seventeen can be regarded as well established.[2]

List of Organic Nitrogenized Substances.

Name.	Where found.
Fibrin	Blood, chyle, lymph.
Albumen	Blood, chyle, lymph, serum, milk.
Albuminose	Chyme, blood.
Caseine	Milk.
Mucosine	Mucus.

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[1] These are called by the French Fibrine and Albumine, but they are more commonly known in English as Fibrin and Albumen.

[2] Traité de Chimie Anatomique, etc., par Ch. Robin et F. Verdeil. Paris, 1853.

Name.	Where found.
Pancreatine	Pancreatic juice.
Globuline	Blood-globules.
Musculine	Muscles.
Osteine	Bone.
Cartilageine	Cartilage.
Elasticine	Elastic tissue.
Keratine	Nails, hair, epidermis.
Crystalline	Crystalline lens.
[1] Hematine	Colouring matter of the blood.
Biliverdine	" " " bile.
Urosacine	" " " urine.
Melanine	" " " pigment.

Of the seventeen principles above enumerated, only three have been studied with any degree of accuracy; namely, fibrin, albumen, and caseine. The proportion of these elements in the fluids in which they have been found has been carefully estimated, and, in addition, much pains have been bestowed upon their ultimate analysis. Albumen, the one with which we are most familiar, has given the name to all these substances, from similarity, as far as known, of composition, &c., and the remainder, thus called *albuminoids*, have been simply indicated in the situations above enumerated, no attempt having been made, with one or two unimportant exceptions, to estimate their quantity or ascertain their ultimate composition. In fine, the blood and the milk are about the only fluids of the body which have been subjected to critical analysis for organic substances; and hardly anything has been done with the solids. I do not propose in this article, to take up the chemistry of the milk, and, throwing out this fluid, I am reduced in my examination of analyses to the organic elements of the blood, which has justly claimed the most careful investigation at the hands of the physiological chemist.

In the latter part of the last century, Berthollet discovered the existence of nitrogen in organic bodies. Before his time chemists had little idea of their composition. It was known that they were very unstable, and the discovery of the above-named ingredient offered a supposed explanation of this fact; *i. e.*, that its presence engendered a number of "attractions" which did not operate in bodies of a less complicated composition. This discovery was a great step in the chemical knowledge of organic substances of this class; and the researches of investigators since that time have so far established it, that they are known generally under the name of *nitrogenized*, or *azotized* principles. The organic matters were then closely studied by Dumas, especially those existing in the blood; and, indeed, the mode of analysis of this fluid for its organic ingredients employed by Dumas forty years ago, is the one adopted, with but slight modifications, by chemists of the present day. He ascertained, in the first place, the amount of water which could be driven off from the blood, and attributed it all to the serum, considering the fibrin and albumen as held in solution by this water, and the globules as possessing no fluid of their own. By appropriate means, which will be considered hereafter, he separated the fibrin, albumen, and globules, evaporated them to dryness, and estimated them in this condition. The ultimate composition of these principles was not then definitely ascertained, and no theory of the mode of union of their elements or their formation was proposed. A few years later (1837), in connection with Liebig, Dumas proposed a division of chemical science into inorganic or mineral, and organic. According to the theory thus proposed, all inorganic bodies were composed of two elements directly combined, forming what they called binary compounds, which again united with other compounds formed in the same way. Thus, potassium and oxygen united to form potash (KO), which, in its turn, may unite with another binary compound, as nitric acid (NO_5), to form nitrate of potash (KO,NO_5); the elements first uniting together to form pairs, which, in their turn, unite with each other. In inorganic chemistry the union of elements proceeds, in this simple manner, to form the most complex substances; an element can only unite with an element, a binary compound with a binary compound, and so on. Organic, particularly vegetable substances, on the contrary, were theoretically reduced to the compounds of a radical which, though itself a compound, behaved towards elementary substances in the same way as a simple inorganic element. In other words, the behaviour of these so-called organic radicals in their union with elementary substances would lead us to suppose them to be elements themselves; it is only chemical analysis which shows them to be compound. For example, cyanogen will unite with hydrogen to form hydrocyanic acid (HCy), as chlorine will unite with hydrogen forming hydrochloric acid (HCl). The latter is an inorganic or mineral acid, and the chlorine, which is the radical, is of necessity an elementary substance; but cyanogen, the radical of the organic acid, though it unites with the element hydrogen in the same way as the chlorine, behaving like an elementary substance, is found by chemical analysis to be a compound of carbon and nitrogen (C_2N). It is in reality a radical, but compound, and a compound radical is a thing unknown in inorganic chemistry. The example just given shows a marked difference in the behaviour of inorganic and organic substances, as the radical C_2N, or cyanogen, actually exists and conducts itself, as we have seen, not as a compound, but an elementary substance; and if all organic compounds could be shown to be formed of compound radicals, this would constitute a true distinction between mineral and organic combinations. But this is not the case; though some chemists have theoretically reduced alcohol, ether, acetic acid, and in fact all organic vegetable compounds, to a union of elements with compound radicals, the radicals, unlike cyanogen, are hypothetical. It is said, for example, that the radical ethyle

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[1] These are simply colouring matters, and are put by Robin and Verdeil in this class, as they contain nitrogen.

(C^4H^5) unites with oxygen to form the oxide of ethyle (C^4H^5O), which is ether; with oxygen and an equivalent of water, to form the hydrated oxide of ethyle (C^4H^5O+HO), in alcohol, etc. etc., but ethyle never exists in nature, and cannot be manufactured. The same is true of the radicals, methyle, acetyle, benzoile, ammonium, &c. The hypothetical character of these radicals is universally acknowledged,[1] and the theory of compound organic radicals, though it may serve to explain the composition of certain classes of organic bodies, is not universally received by chemists of the present day; it is rather a mathematical analysis than an actual investigation of real substances; for, with the exception of one or two, *all the radicals are hypothetical.* This wholesale assumption of imaginary substances violates, *in toto*, the principle enunciated at the beginning of this article. Instead of studying the phenomena of organic bodies, phenomena are imagined and facts distorted to correspond to the laws which are known to regulate the behaviour of inorganic substances. But it is beyond the scope of this paper to treat of these purely chemical questions; the reason the theory of organic radicals has been discussed at all is, that it was followed the next year, 1838, by the theory of Mulder, by which he attempted to explain the constitution of the albuminoids. He supposed all organic nitrogenized substances in the body to be formed by the union of certain elements with a radical, *proteine*, giving to them the name of proteine compounds. This hypothesis was adopted by Liebig, Dumas, and Simon, and is now accepted by many physiologists. It is then one of the most important questions which we have to discuss in studying the composition of organic nitrogenized bodies.

Proteine.—As before remarked, the only albuminoids that have been carefully studied are fibrin, albumen, and caseine. In addition to a great similarity in the general properties of these substances, ultimate analysis has shown a remarkable likeness in chemical composition. It is not to be wondered at, then, that an attempt should be made to reduce all the compounds of this class to a series derived from a common radical, following upon the theory of organic vegetable radicals, which was first pretty generally received. This was done by Mulder; who, treating albumen, fibrin, or caseine with alcohol and ether to remove the fats, and with hydrochloric acid to remove inorganic salts, dissolved these substances, thus purified, in a solution of potash, and precipitated by acetic acid a substance said to possess always the same characters, which he called the radical of the albuminoids, and which, by union with a certain quantity of sulphur and phosphorus, was capable of forming fibrin, albumen, or caseine. This, which is merely an extension of the theory of compound organic radicals into animal chemistry, has a more plausible basis than in the formation of vegetable organic compounds. The supposed radical proteine was obtained and analyzed by Mulder; and if it could be definitely established to be the same for the various substances from which it is extracted, and if these substances could be shown to consist always of this radical with a definite proportion of sulphur, or sulphur and phosphorus, the theory would be sustained, as far as possible with our present means of investigation. It is true it would only be sustained by analysis, but synthesis cannot yet, if indeed it ever can, be applied to animal chemistry; for we have thus far been unable to construct a single organic principle of the body out of its elements. But the proteine theory is not susceptible of analytical demonstration. The composition of proteine itself is not definitely settled; and when we come to review the methods of ultimate organic analysis, we will see that the varied results obtained by chemists do not depend on a want of accurate means of analysis, but upon the indefinite characters of the compounds themselves. Let us take, for example, the analyses of Mulder[1] showing the composition of the proteine groups, and compare them with the results obtained by other chemists!

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[1] For a *résumé* of the history of these so-called organic radicals the reader is referred to a lecture by M. Auguste Cahours, published by the Société Chimique de Paris, 1860, p. 51.

Mulder gives the following formulæ for the proteine group:—

$C^{40}H^{31}N^{5}O^{12}$ = Proteine.
$C^{40}H^{31}N^{5}O^{12} + SPh\frac{1}{2}$ = Fibrin and albumen of white of egg.
$C^{40}H^{31}N^{5}O^{12} + S^{2}Ph\frac{1}{2}$ = Albumen of serum.
$C^{40}H^{31}N^{5}O^{12} + S$ = Caseine.

This analysis of Mulder has been confirmed by Schröder and Von Laer.[2] Regnault gives as the constitution of proteine $C^{30}H^{23}N^{4}O^{10}$;[3] Sheerer, $C^{48}H^{72}N^{12}O^{14}$;[4] Liebig, $C^{48}H^{36}N^{6}O^{12}$; and Dumas, $C^{48}H^{35}N^{6}O^{17}$.[5]

The composition of fibrin, albumen, and caseine given by Dalton, and credited to Liebig, is as follows:—[6]

Fibrin = $C^{298}H^{228}N^{40}O^{92}S^{2}$
Albumen = $C^{216}H^{169}N^{27}O^{65}S^{2}$
Caseine = $C^{288}H^{228}N^{36}O^{90}S^{2}$

Denis, in a paper presented to the Academy of Sciences at Paris in 1839, advanced the view that fibrin and albumen are identical in composition; which view was sustained by Liebig in a note to the Academy in 1841.[7]

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[1] Robin and Verdeil, Chimie Anatomique, tome i. p. 652.

[2] Animal Chemistry with reference to the Physiology and Pathology of Man. By Dr. J. Franz Simon. Philadelphia, 1846.

[3] Cours Elémentaire de Chimie, etc. Par M. V. Regnault. Paris, 1853, tome iv. page 114.

[4] Milne-Edwards. Leçons sur la Physiologie, etc. Paris, 1857, tome i. p. 151.

[5] Robin and Verdeil, op. cit., tome i. p. 651.

[6] Dalton's Treatise on Human Physiology. Second edition. Philadelphia, 1861, p. 80; and Robin and Verdeil, op. cit., tome iii. p. 147.

[7] Robin and Verdeil, op. cit., tome iii. p. 282.

With this diversity of opinion among chemists, based on actual analysis, it is impossible to come to any other conclusion than the following:—

There is no evidence that fibrin, albumen, and caseine are formed by the union of a *definite proportion* of phosphorus and sulphur with a common radical.

In addition it is certain, if we attach any weight to ultimate analyses, that the properties of these substances do not depend entirely on their chemical composition. If we look at the analyses of Mulder, even, we find that two substances as dissimilar as it is possible for substances of this class to be, namely, albumen of the white of egg and fibrin, have the same ultimate composition. The minute composition then does not seem to be important as regards the general properties of the compound. Let us now see whether this composition be invariable or not; whether, in other words, these compounds are not of *indefinite chemical composition.*

Notwithstanding all the labour which has been bestowed upon the ultimate analysis of the substances under consideration, the question of their composition does not seem to be one of any great importance. The difficulties of such an analysis, and, as we have just seen, the contradictory results in the hands of skilful chemists, show that a knowledge of the ultimate composition of organic nitrogenized substances is of little value as a means of distinguishing them from each other; and such an analysis throws no light whatever on their function in the economy. A careful review of the facts which have been accumulated on this subject leads to the conclusion that *these bodies are of indefinite chemical composition.* In the first place they are not crystallizable; secondly, they may be made to assume different forms and properties by the action of imponderable agents, as in coagulation by heat or galvanism, without losing or gaining any elements; thirdly, they are in a continual state of change, in nutrition during life, without losing their properties, and will continue to absorb oxygen and exhale carbonic acid for some time after removal from the body,[1] and shortly after these properties have ceased, undergo the changes of putrefaction; lastly, there is no great difference between them in chemical composition, and almost all the analyses made by chemists of equal skill present great variations. Is there not, then, every support for the assertion that their chemical composition is indefinite? Either this assertion is correct, or the methods of analysis employed are inaccurate. As so much depends upon this point, I will venture to give a rapid sketch of the method of analysis most commonly employed by chemists.

It is first ascertained, by a very simple process, that a given substance, say albumen, is composed of certain elements, as carbon, hydrogen, oxygen, nitrogen, sulphur, and phosphorus. This being determined, it is deprived of moisture; the fat is removed by ether and alcohol; and the earthy salts, as far as possible, by dilute hydrochloric acid. A carefully weighed quantity is then decomposed, and the proportions of these elements determined, in the following way:—

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[1] G. Liebig has demonstrated the fact that the muscles of the frog will continue to absorb oxygen and exhale carbonic acid after they have been separated from the body, so long as they retain their contractility. Lehmann's *Physiological Chemistry*, Philadelphia edition, vol. ii. p. 474.

Mode of Analysis.—A tube of the hardest glass, a half an inch in diameter, sixteen to eighteen inches long, and closed in a flame at one end, is used for the decomposition, which is effected by combustion. The oxidation is effected by means of the black oxide of copper, which is prepared for the purpose perfectly pure, carefully powdered, and freed from every particle of moisture. The tube is first filled for two or three inches with pure oxide of copper. The organic matter is now to be carefully powdered, incorporated with oxide of copper (it is best to employ from five to eight grains of organic matter for the analysis), taking care that not a particle be lost, and the mixture introduced into the tube. The tube is now to be filled to within an inch of the extremity with the pure oxide of copper.

In performing this part of the manipulation, care should be taken to remove all moisture, as this would affect the quantity of hydrogen obtained from the combustion. This may be done by attaching the tube, after it has been filled, to one opening of a small air-pump, such as is used for this purpose, the other being fitted to a bent tube filled with pumice stone and sulphuric acid. By placing the combustion tube in a long dish filled with warm water and exhausting the air a few times, all the moisture may be removed.

As the tube is to be subjected to considerable heat, it is best to wind it with a narrow ribbon of sheet brass, which will prevent its bending when it becomes softened. We now attach to the open end, by a smaller tube fitted perfectly with a cork, a light tubular apparatus filled with small fragments of chloride of calcium, the tube and its contents having been previously weighed, and we connect with this a series of bulbs, called Liebig's potash bulbs, partly filled with a solution of caustic potash, which is likewise carefully weighed. The heat may now be applied to the combustion tube, which may be done in a long glass furnace made for the purpose, or by surrounding it, well supported in a long iron trough, with hot coals. The heat is applied gradually, beginning at the nearer end of the combustion tube. The organic substance is thus completely decomposed, and if it were composed of carbon, hydrogen, and oxygen, like sugar, the analysis would be complete—this combustion giving us the carbon and hydrogen, and the oxygen being obtained by difference. As it is, all the hydrogen is converted into watery vapour, which is absorbed by the chloride of calcium, and the carbon, converted into carbonic acid, is absorbed by the potash. The weight of these products is ascertained by taking the increase of weight of the calcium tube and the potash bulbs, and the quantities of *carbon* and *hydrogen* are deduced therefrom.

We have now remaining the nitrogen and sulphur. We may use the same tube, with a little modification, for carbon, hydrogen, and nitrogen; but it is better to estimate the latter in a new apparatus. For this purpose we take a combustion tube similar to the one just described, placing at the closed end a few grains of bicarbonate of soda; then the oxide of copper as before; next the mixture of oxide of copper and the organic matter; next another layer of pure oxide of copper, and last of all a layer of pure copper reduced by hydrogen. The extremity is then connected with one opening of the air-pump, and to the other is adapted a tube which opens under a receiver containing mercury with a solution of potash floating on the top. We then exhaust the air as completely as possible and connect the combustion tube with the receiver by opening both stopcocks of the air-pump. It is necessary now to drive out all the air from the apparatus, as we wish to collect the nitrogen in a gaseous form. For this purpose we apply the coals to the further extremity of the tube, when the heat decomposes the bicarbonate, and carbonic acid gas is evolved. We see that all the air is driven off, by the complete absorption of the gas evolved by the potash in the receiver, showing that pure carbonic acid is coming over. We then substitute another receiver filled with mercury and a solution of potash, withdraw the heat from the bicarbonate, and apply it gradually from the anterior portion of the tube as before. Combustion of the organic matter takes place, which results in watery vapour, carbonic acid, which is absorbed by the potash in the receiver, and nitrogen, which passes over and is collected in a gaseous form. Some of the nitrogen is oxidized by this combustion, but as it passes over the hot metallic copper in the nearer extremity of the tube, the oxygen is retained and the nitrogen passes over pure. After the combustion of the organic matter is complete we again apply heat to the bicarbonate of soda so as to drive off what nitrogen remains in the tube by the evolution of carbonic acid. We then remove the receiver, substitute water for the mercury, measure the volume of the gas, taking the temperature carefully and bringing the level of the water in the tube to that of the surrounding liquid; thence deduce its weight, which gives us the proportion of *nitrogen*.

The sulphur and phosphorus, if there be any, exist in very small quantity. They may be estimated in the albuminoids without any great difficulty, by causing them to unite with soda, as sulphuric or phosphoric acid, and then precipitating with the chloride of barium for the sulphur, and by a process a little more complicated, but not less exact, for the phosphorus, which it is not necessary to describe here.[1]

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[1] An admirably clear exposition of the whole process for the analysis of organic substances, with all the precautions for making it perfectly accurate, is found in Regnault's *Cours Elémentaire de Chimie*, tome iv. p. 9 et seq.

We have thus obtained the weight, in a given portion of albumen, of all its ingredients but the oxygen, *i. e.*, carbon, hydrogen, nitrogen, and sulphur. By subtracting the sum of the weights of these substances from the whole weight, we have the oxygen; and reducing to 100 parts we have the ultimate composition.

I have given the process rather fully, to show how, with certain precautions, in the hands of one skilled in chemical manipulations, it may be made as accurate as any operation in inorganic chemistry. With a balance that will turn with less than $\frac{1}{1000}$ of a gramme, and with care to avoid moisture, etc., in the apparatus, the result should be always the same, if the substance analyzed had always the same composition.

The next step is to establish the formula in equivalents. If the substance used were an acid or a base, which combined with any substance of known combining equivalent, this would be easily done, by getting the weight of a combining atom by experiment, calculating the proportions of its ingredients to this weight, and dividing the quantity of each element thus obtained by its combining equivalent. But in the case of the albuminoids, which are neutral, this cannot be done.[1] A formula is calculated for them which ex-

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[1] The following extract from a note from Prof. B. Silliman, Jr., of New Haven, which he has kindly permitted me to publish, gives the views of this eminent chemist on the important question of the determination of formulæ for the albuminoids.

"If I understood correctly your inquiry the other day respecting the formulæ of the albuminoid substances, the difficulty in your mind was, to determine on what principle a given formula was selected from a certain ratio of numbers. There is, in truth, a serious difficulty in stating the formulæ of all organic bodies; but there are, nevertheless, certain general rules which guide the chemist in such cases. Take, for example, the composition of *alcohol*, the commonly received formula of which is $C_4H_6O_2$. The percentage composition is of course very easily ascertained from this formula, thus

$$C_4 \quad H_6 \quad O_2.$$

$$24+6+16=46.$$

$$46:24=100:x=52.18 \text{ per cent. of Carbon.}$$

$$46:\ 6=100:x=13.04 \text{ `` `` `` Hydrogen.}$$

$$46:16=100:x=34.78 \text{ `` `` `` Oxygen.}$$

"But it is plain that any multiple or submultiple, of the established formula for alcohol will present the same *ratio*; thus we may have

$C_2\,H_3\,O$

$C_4\,H_6\,O_2$

$C_6\,H_9\,O_3$

$C_8\,H_{12}O_4$, &c.

"Which shall we select? Usually the simplest, or that which gives the smallest number of whole equivalents. But in case of bodies which, like alcohol, are volatile, we have a specific guide in the *vapour density*, which will vary, of course, presses the elements in the simplest manner so as to give no fraction, and generally giving an even number for the atoms of carbon.[1] Thus Liebig gives the formula of fibrin $C^{298} H^{228} N^{40} O^{92} S^{12}$.

This review of the mode of ultimate analysis of organic nitrogenized bodies, makes it evident to any one in the slightest degree conversant with chemical manipulations, that the contradictory results obtained by different chemists are not due to imperfections in the analytical process; indeed, the process is acknowledged by chemists generally to be as accurate as that for the determination of the composition of inorganic substances. The only way, then, to explain the contradictory results obtained by different chemists of equal skill and reputation, is to assume that the chemical composition of the principles is indefinite. While enough has been said to convince the reader of this fact, it follows that important results are to be expected rather from a study of the condition and behaviour of these substances in the economy, than their decomposition into elements. When they have been extracted from the body, they are by no means in the condition under which they normally exist. This being the case, it is for the physiological chemist to give their quantity, properties, etc., as far as he can, *in the condition in which they really exist in life;* the physiologist then takes them and studies the vital phenomena in which they are concerned. Here comes the important question: *What is the condition of existence of the organic nitrogenized elements in the body?* On the answer to this question depends the mode of proximate analysis of the organized fluids of the body, especially the blood, which is all important to the physiologist.

Condition of Existence of Organic Nitrogenized Substances in the Body.—In the ordinary proximate analysis of the blood, by which is meant

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with the number of equivalents, and serves as a definite control over the symbol or formula.

"As regards the composition of the albuminoids, you will remark that they are all derivatives of cellulose by removal of three equivalents of water, and the substitution of three equivalents of the elements of ammonia. Thus $C_{24}H_{20}O_{20}+3NH_3=6H_2O_2+C_{24}H_{17}N_3$. This view, first presented in 1845, in my *First Principles of Chemistry*, by Mr. Hunt (pp. 512, 513, edition of 1852), coincides in a very remarkable manner with the best analyses of fibrin and protein by Mulder. By it protein is a nytril or amid of Cellulose, and in accordance with this, when protein is dissolved in concentrated hot chlorhydric acid, it yields ammonia (as sal ammoniac), water and a brown insoluble substance identical with that resulting from the slow decay of wood. This view for a long time lay unregarded, but lately has been brought out again as new by Dusart and other continental chemists. (See *Am. Journ. Sci.*, 1848, vol. v. p. 74; 1862, vol. xxxiii. p. 113.) I commend this subject as therein set forth to your perusal.

"In a physiological point of view, as an example of the results of vital chemistry, the production of albuminoid bodies from cellulose, has always appeared to me to be one of the most interesting topics in organic chemistry."

[1] Regnault, Chimie, op. cit., tom. iv. p. 54.

an analysis giving the proportions of proximate principles without any reference to their ultimate composition, the albumen and fibrin are put down in a very small proportion. Fibrin is recognized by its spontaneous coagulability, and albumen by its coagulability by heat and nitric acid; and we know that the fibrin may be extracted from the blood coagulated on rods, and the albumen of the serum solidified by heat or nitric acid, in quantities which are evidently much greater than those given in analyses. The physician finds it difficult to reconcile to his ideas of albumen and fibrin of the blood, the proportions of sixty to sixty-five parts per thousand for albumen, and two and a half for fibrin. The reason why the estimates fall so far below our ideas, is, that chemists never have estimated the fibrin and albumen as they are separated from the fluids by coagulation, which only changes their form and not their weight; but after separating them in this way, have subjected them to perfect desiccation. We have therefore not the weight of the principles as they exist, not the fibrin and albumen which are calculated to nourish the body, but the desiccated substance, altered, and its properties destroyed, by this process. Physiologists tell us that fibrin and albumen are in solution in the water of the blood, and that their natural condition, in a state of purity, is that of a dry powder. In this case it is extremely difficult to reduce these substances to their natural condition. When we coagulate them, which, according to this view, is a precipitation, a large quantity of water persistently remains in combination with them which it is very difficult to get rid of, and when got rid of, the dry substance must be weighed quickly and with many precautions, to avoid a resorption of moisture. Other matters are also found combined with the coagulated organic substance. All the salts which are found in the blood are united with it as well as the water; and in the proximate analysis, these salts are not generally separated from the organic substance before it is weighed. This view, which is almost universally held by physiologists, is the one which has guided all the analyses which we have of the organized fluids. In the original works to which I have access, that of Robin and Verdeil, on Anatomical Chemistry,[1] is the only one in which I find any dissent from the prevailing doctrine. They regard the organic elements of the fluids as naturally fluid and not in solution; those of the semi-solids as naturally semi-solid; and of the solids as solid. The contrary view seems to me radically and entirely wrong; and all analyses of the organized fluids, made with the idea that organic substances are in solution, fail to give anything like a correct idea of the properties of these substances. The analyses of the blood which are embodied in the latter part of this paper, are the only ones, as far as I know, which have been attempted with reference to the real condition, as it seems to me, of the organic constituents. They have been made on the following principle:—

The water which is contained in coagulated organic substances, which

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[1] Op. cit., tom. iii. p. 121.

may be driven off by dry heat, &c., is not part of the water which held the organic matter in solution, but an actual constituent of the substance, as much as the carbon, hydrogen, or nitrogen, and indispensable to the properties by which we recognize it as an organic principle.

It has already been shown that ultimate analysis does not give us an idea of the distinctive characters of different organic matter. For this we must depend upon certain characters which are found in all principles of this class, and further, upon certain properties which serve to distinguish them one from another; and when deprived of their water of composition by desiccation, neither in their general properties nor in chemical composition do we have any means of recognizing them, unless it be, by their indefinite chemical composition and the impossibility of making them assume a definite or crystalline form.

First, with regard to their general properties. They all undergo a change peculiar to themselves, called putrefaction. This property, which is the one perhaps most distinctive of organic matter, is abolished when they are deprived, even partially, of water; a fact which is well known and of which we have a familiar example in the preservation of meat. Again, when an organic substance is in a state of putrefaction, it is capable of inducing the same change in other elements of this class by what is called catalysis, or acting as a ferment. As water is necessary to putrefaction, it is consequently necessary to the development of this property. Principles of this class also undergo a change peculiar to themselves in cooking; which is characterized by the development of volatile empyreumatic substances. Water is necessary to this change, for if exposed to heat after water has been driven off, as has already been seen in the study of the mode of ultimate analysis, they are resolved into their elements without undergoing any such change. They also are capable of regaining their water of composition after desiccation, possessing to an eminent degree what is called the property of hygrometricity, by which they are returned to the condition they assumed when first coagulated. This coagulability is also a peculiar property, and entirely different from precipitation from a solution. They cannot be redissolved in the fluid from which they are separated by coagulation. For example, albumen, and indeed all of them are insoluble in alcohol; but if albumen be coagulated by alcohol, and afterwards freed from it, it cannot be redissolved by pure water, or the fluid from which it was separated. When once coagulated they have undergone a change, and cannot be redissolved except by means which change them still more. When they have been coagulated and dried, reduced to what is called a condition of purity, they cannot be redissolved and detected by their property of coagulation, for they are changed, and consequently not in their natural condition.

When we are asked what we mean by fibrin, we answer that it is an organic constituent of the blood, which possesses the property of coagulating when removed from the body, giving this property to the whole mass of blood, which separates, after a time, into clot and serum. We would define albumen as a principle of the same class, existing in the serum, which is coagulated by heat or nitric acid. These are naturally fluid, but coagulate, in the one instance spontaneously, and in the other by the means just mentioned. We cannot say that they are principles composed of so many atoms of carbon, nitrogen, &c., because their composition is indefinite. If asked the proportion of these principles contained in the blood, we can only say that after they have been separated from this fluid, and after all their water has been driven off, there have been found $2\frac{1}{2}$ parts of fibrin, and 60 or 70 of albumen per 1000. This latter answer conveys to us no idea of the real quantity, for we care nothing about the quantity of anhydrous matter contained in these substances, we wish to know the quantity of *coagulating* fibrin and albumen found in the blood. Analyses giving the quantities of these substances as near as possible in their natural condition, have never been made, though they would seem the only ones which could convey any definite idea of what we wish to know. I have attempted to supply this deficiency, to a certain extent, in Part II., on the Analysis of the Blood, or at least to show what we wish to ascertain.

I have enumerated about all the properties by which we recognize organic nitrogenized substances, separated from the living organism, as a class; namely, putrefaction, the property of becoming ferments, changes in coction, desiccation, hygrometricity, and coagulation; and all of these depend on the presence of water. Should we not, then, almost conclude from these facts that water is a necessary and very important element of their constitution! It is true that it is separated with great facility, and that its union with the other ingredients is not very powerful; but this is no argument against the fact of its being in a state of positive union. There are many substances in the inorganic world which have a union no more powerful than that of water in organic matters. Take the single example of the bicarbonate of soda. The second equivalent of carbonic acid is driven off by a gentle heat, and even by exposure to the air at the ordinary temperature, leaving the salt in the condition of a carbonate.

There is another circumstance in connection with the mode of union of water with other ingredients to form an organic body which serves to distinguish it from mere solution. When a solid substance, as a salt, is in solution in any fluid, it requires a certain quantity of the fluid to dissolve a certain quantity of the solid, but beyond this the fluid may be increased indefinitely; the solid having the same relation of solution to the whole mass. On the contrary, when one chemical compound, as sulphuric acid, unites with another, as with soda, one equivalent of the one combines with one equivalent of the other, and if more of either one be added, it does not enter into combination. Now I regard the organic substances found in the fluids of the body as naturally fluid, and mixed with the other fluids; the water which enters into their composition, as represented by the water which they contain when separated from the other fluids by coagulation; and this quantity of water, though not absolutely definite, is as definite in its proportion as the other ingredients. It is restricted within definite limits; and though, when fluid, like many other fluids, it may be mixed with an indefinite quantity of water, when separated by coagulation water will always be found in about the same proportion.

There is another point of view, by far the most important physiologically, from which we must study this question of the natural condition of the organic ingredients of the fluids. Do they conduct themselves in the vital operations of nutrition like the inorganic substances, which are undoubtedly held in solution, or like substances naturally fluid?

This question seems to me very easily answered. The processes of nutrition of the organic elements of the body consist in a change of the fluid organic substances, principally the albumen and fibrin, into those which are semi-solid and solid, like musculine, osteine, etc. In the process of these changes, water is of course absolutely necessary, and is deposited with the other elements of the organic matter. It, as well as the carbon, hydrogen, oxygen, and nitrogen, is necessary to the constitution of the musculine and osteine, and is involved in all the catalytic changes of nutrition.

Having special reference to the blood, and the organic substances which it contains, the relations between this fluid and the tissues constitute one of the most important and interesting of physiological inquiries. In the organic elements of the solids and semi-solids of the body reside, undoubtedly, the vital properties which lead them to regenerate themselves at the expense of the circulating fluid; and in the tissues and organs, as well as the blood, the organic matters are always united with inorganic salts, as well as water. Of these salts, some, in connection with organic matter, go in great measure to make up the tissues, as the phosphate of lime in the bones; while others seem by their presence to regulate somewhat the nutritive processes, like the chloride of sodium, which is more abundant in the blood than in any of the tissues. It is an invariable law that organic nitrogenized principles, whether fluid, semi-solid, or solid, never exist alone, but always in combination with inorganic substances. It is impossible, indeed, in extracting the organic substances from the body, to free them entirely from inorganic salts; and the fibrin and albumen of the blood I have found to contain all of the salts which exist in that fluid. The blood contains all of the elements, both organic and inorganic, which are necessary for the regeneration of the tissues. The inorganic elements are deposited unchanged, and in the organic elements alone resides that property of mutual convertibility which forms musculine, cartilagine, osteine, etc., out of albumen and fibrin. In this process of change we have a deposition of the salts, which cannot take place by itself, but must be involved in the deposition of organic matter. This process is not to be explained by the laws of chemical attraction, nor represented by a change in chemical formulæ. It is an act which takes place only in organic living bodies, and the more we attempt to elucidate it by investigations of a purely chemical nature, the further we remove ourselves from a comprehension of the essence of nutrition. We must learn to look on processes like this as physiological and not chemical; and as we never have constructed, and perhaps never will construct, a single organic nutritive substance out of its elements, nor changed one into another, so we will ever fail to comprehend the phenomena of change and the mystery of their construction in the body, if we persist in endeavouring to adapt these phenomena to the laws which regulate the composition and changes of inorganic substances. When we study the composition of these substances, we should take them as we find them, and not try to reduce them to a condition approximating that of minerals. The absence of useful results following the labours in this direction of so many chemists should be a warning to us to quit the beaten track. When we study their properties, we have already seen that it is necessary to take them as they are, combined with water, or these properties are lost. When we come finally to study their vital functions in the economy, we find that they not only contain water, but inorganic substances, which are indispensable to the great function of nutrition, and which cannot be separated from the organic. We must in this study recognize the following important facts.

First. Organic nitrogenized substances are the only elements of the body in which reside the properties of destruction and regeneration during life. Fats, sugar, and inorganic salts operate with them, and by virtue of this property, which we may call vital.

Second. They are of indefinite chemical composition; and no physiological importance is to be attached to ultimate analyses. They are unstable; in a state of continual change during life, and soon alter after death, or after being removed from the body.

Third. They assume the consistence of the tissue or fluid in which they exist. They are solid in the solids, like bone; semi-solid in the semi-solids, like muscle; fluid in the fluids, like the blood. They are not dissolved in water, but water is an ingredient, and its quantity determines their consistence.

Fourth. In the body they never exist alone, but always combined with inorganic substances, which accompany them in the changes they undergo in the processes of nutrition and destructive assimilation.

Fifth. As all the proximate analyses of the organized fluids, particularly the blood, have been made with the idea that the organic ingredients were solids in solution in water, these quantitative analyses give, not the proportion of fibrin or albumen, but dried fibrin and albumen, the original substance subjected to a process which drives off its most important constituent, and which alters its properties. Such analyses, as representing real quantities, are erroneous.

PART II. *Analysis of the Blood with special reference to its Organic Constituents.*—From the review we have given of the organic constituents of the body, and the intimate relation we have seen to exist between the tissues and the blood, it becomes evident that an analysis of this great nutritive fluid, especially with reference to its organic constituents, is of the highest interest and importance. This fact has long been recognized, and of late years a great part of the labours of investigators in physiological chemistry have been devoted to this subject. It is not my purpose here to consider any but the organic principles of the blood. The constitution of this fluid, in its entire physiological and pathological relations, is too extended a theme to be considered in this place. The fact that the blood contains certain excrementitious substances shows that this fluid is connected with the waste as well as the repair of the system. The pathological importance of this has been settled experimentally by the discovery of the accumulation of these excrementitious elements in the circulating fluid, giving rise to certain pathological conditions; as, for example, the urea, producing a condition of the system known under the name of uremia; and more lately, the discovery of the character of cholesterine as an excretion and its accumulation in the blood, under certain conditions of the liver, constituting cholesteremia.[1] These are only two examples where diseased conditions of the system have been clearly shown to depend upon the accumulation of a specific excrementitious substance in the blood, acting as a poison; but the work in this direction is but begun; and I venture to predict that more light will be thrown on pathology by the discovery of new poisons in the blood, dependent on defective excretion, than by any other line of experimental inquiry. There are already some known excrementitious substances, creatine and creatinine, for example, of the pathological relations of which we are entirely ignorant; and we must look to these and other elements of this class, which may be discovered hereafter, for light on the pathology of many diseases now obscure.

The proximate analyses of the blood up to this time, have been made under the supposition that the organic matters, fibrin and albumen, were solid elements in solution; but according to the views advanced in Part I, namely, that their real condition is one of fluidity, and that when deprived of water they lose one of their most important ingredients, this mode of analysis is inadmissible. The real quantities of fibrin and albumen can no more be represented by the residue of evaporation, than by the residue of calcination, which would leave only inorganic matter. Before giving, however, the processes by which I have attempted to estimate the quantities of *undried* fibrin, albumen, and globules in the circulating fluid, let us take a rapid review of the methods of proximate analysis which are now generally employed.

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[1] See an article on a "New Excretory Function of the Liver," by the author, published in the number of this Journal for October, 1862.

Berzelius, followed soon after by Marcet, gave us the first quantitative analyses of the blood. He analyzed the serum of the human blood, and indicated certain quantities of albumen, lactate of soda, muriate of soda, etc. He put the quantity of dried albumen at 80 parts per 1000, which is about the proportion given in the analyses of chemists of the present day. His researches were published in 1808, and were followed by the analyses of Marcet in 1811, which gave about the same results. In 1823, Provost and Dumas published their researches on the composition of the circulating fluid, with a full account of their process. This process, with slight modifications, is the one employed generally at the present time. The following are the principal steps in the analysis of these eminent investigators: The fibrin is separated from a weighed quantity of blood by whipping with a bundle of broom-corn, carefully collected, dried, and weighed. Another specimen of blood is set aside to coagulate, and after it has fully separated into clot and serum, the clot is dried and weighed; the proportion of fibrin ascertained by the first specimen is subtracted, which gives the quantity of dried globules. The serum is then evaporated to dryness, the residue extracted thoroughly with boiling water, ether, and hot alcohol to remove the inorganic salts and fat, and afterwards weighed, which gives the proportion of albumen. The fats are easily extracted with ether, and the inorganic constituents estimated after incineration, by a process which it is not necessary to describe. Reducing all these results to 1000 parts, we have a table of the constitution of the blood.

This process has been followed, with unimportant modifications, by a number of distinguished chemists, who have done little more, with regard to the albumen and fibrin, than confirm the observations of Provost and Dumas. Among these may be mentioned Andral and Gavarret, Becquerel and Rodier, Sheerer, and Simon. Among these observers, perhaps, the process adopted by Becquerel and Rodier is one as generally accepted by physiologists as any, and I will therefore translate from their excellent work, entitled *Traité de Chimie Pathologique,* so much of it as refers to the estimation of the fibrin, albumen, and globules.

"*First Series of Operations.*—This is designed to furnish: First, the density of the blood and that of the serum; second, the weight of fibrin, globules, and that of the solid matter of the serum taken as a whole. These processes are founded on the same principle which served as the basis of the process devised long since by M. Dumas. We suppose that all the water contained in the blood forms part of the serum, and should be attributed to it. Still, in admitting this principle, we have not always applied it in the same manner.

"The following is our mode of operation:—

"We practise upon the person whose blood we wish to analyze, a bleeding of about 375 grammes.[1] The blood which first flows from the vein is received in a glass vessel, graduated, and capable of holding about

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[1] A gramme is a little more than 15 grains.

125 cubic centimetres of this liquid. We collect it and whip it with a bundle of broom-corn. We thus obtain the fibrin, which we must wash, desiccate, and weigh.

"The blood, thus defibrinated, is then put aside to serve for other operations.

"The blood which flows from the vein, after these 125 cubic centimetres, is collected with care in a vessel of the capacity of 250 to 300 cubic centimetres and left to itself. This blood coagulates, and once the coagulation effected, we separate carefully the serum, which we put aside in a vessel; as to the clot, after having taken note of its physical characters, we may set it aside.

"Let us see now what we do; first, with the defibrinated blood; second, with the serum.

"A. The *defibrinated blood* is first weighed at a definite temperature in a glass specific-gravity bottle.[1] We compare then the weight which we obtain in this operation with the weight of the same volume of distilled water; and we thus have, by a very simple calculation which it is useless to reproduce here, the exact weight of the 125 cubic centimetres of blood which we whipped to separate the fibrin, and consequently the weight of this same fibrin contained in 1000 grammes of blood. Once this operation effected, we take a definite quantity of defibrinated blood, which we weigh, which we desiccate, which we afterwards weigh anew, and we thus have the weight of the quantity of water which it contains. Let us take, for example, in order to make ourselves better understood, arbitrary numbers which we will make use of also to deduce the weight of the globules: 100 grammes of defibrinated blood, liquid, gives 20 parts of solid material and 80 parts of water. Then 20 parts, thus dried, are calcinated to give us the inorganic matters; we will return to this.

"B. The *serum*.—After having determined the specific gravity of the serum, we take a given quantity of this liquid which we weigh, which we desiccate, which we afterwards weigh anew; the difference of these two weights gives that of the water; as, for example, 100 grammes of liquid serum having given 10 grammes of solid matter and 90 grammes of water. These operations terminated, we possess the figures necessary to deduce the weight of the globules and that of the solid matters of the serum contained in 100 grammes of defibrinated blood. Indeed, as all the water of the defibrinated blood should be attributed to the serum, we must make the following proportion:—

$$80 : x :: 90 : 10 \text{ or } x = \frac{80 \times 10}{90} = 8.8 \; gr.$$

"This proportion 8.8 represents the sum of the solid matters of the serum contained in 100 grammes of defibrinated blood, and subtracting that from 20, the weight of this blood desiccated, we have 11.2 which represents the weight of the globules, and in calculating the whole to 1000, we have 1000 grammes of blood, containing:—

Water	800 grammes.
Globules	112 "
Solid matters of the serum	88 "

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[1] All our specific-gravities were taken at a temperature of 12° (53.6° Fahr.) and compared exactly with distilled water at the same temperature.

"The weight of the fibrin has been given by the first operation, and should be added. Its weight is so small in proportion to 1000 grammes of blood, that we may neglect a little correction which we should have to make for the weight of the fibrin in addition to the 1000 grammes of defibrinated blood.

"Such is the first series of operations; for the second we will make use of the dried serum, and for the third,[1] of the defibrinated blood calcinated.

"*Second Series of Operations.*—These operations are designed to give the weight of the extractive matters and that of the fatty matters. The following is our mode of operation:—

"The serum, having been dried with precaution in an *étuve*, and pulverized with the greatest care, is treated repeatedly with boiling water until this water has completely freed it from everything which it can dissolve. These last are, on the one hand, extractive matters, such as osmazome, the colouring matter of serum, etc. etc., and on the other hand, the salts which are in solution in the serum and are in a free state.

"The serum, thus extracted with water, is dried again and weighed, the difference with the weight obtained by the first weighing indicates that of the matters we have mentioned and which the water has removed. The product of the second desiccation is then treated by boiling alcohol at 90°, until it is completely extracted. The insoluble residue is pure albumen, of which we may take the weight after having dried it. As to the boiling alcohol, it holds in solution all the fatty matters, which can be separated by employing the process indicated by M. F. Boudet, and of which we think it unnecessary to give a description. It gives the seroline, cholesterine, and saponifiable fats."[2]

The above quotation gives a fair representation of the mode of analysis most commonly made use of at the present day. It differs, however, very little from that indicated by Dumas. There are certain objections to this process, aside from those which have reference to the estimation of fibrin and albumen, which have long engaged more or less the attention of physiological chemists and are universally acknowledged to be well founded. It will be observed that all the water is attributed to the plasma while the globules are estimated dry. This is manifestly faulty, as the most cursory microscôpic examination of the blood-globules is sufficient to convince any one that they have a consistence dependent upon the presence of a certain quantity of water; and though it may be convenient to estimate these bodies dry, such an estimate gives no idea of their real proportion. This was appreciated as long ago as 1828, by Denis, who attempted to give the proportions of moist globules by a process which had avowedly little accuracy and which he afterwards abandoned for the original process of Dumas.[3] In 1844, Figuier published an analysis of the blood which allows an estimation of the moist globules by a process which I have employed in the analyses which follow, and which seems to me to give sufficiently accurate results, though Denis does not consider it superior to his own. This process was accepted by Dumas with some modifications which are described by him in the *Annales de Chimie et de Physique* for 1846, p. 452. The process of Figuier depends on the property which certain saline substances have, mixed with the blood, of retaining the globules on a filter. The modification of Dumas is intended to avoid a difficulty which sometimes occurs from alteration and liquefaction of the globules, by which some pass through the filter and are lost. It consists in passing a continuous current of air through the filtering fluid, which prevents this change. In the analyses I have made I have not found it necessary to adopt this precaution.

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[1] This is to ascertain the proportion of inorganic salts.—A. F., Jr.

[2] Becquerel and Rodier, op. cit., page 21.

[3] Mémoire Sur le Sang. Par P. S. Denis (de Commercy). Paris, 1859, p. 51.

The following is the process described by Figuier translated from the *Annales de Chimie et de Physique.*[1] It was not used by him to determine the proportion of *moist* globules; the globules are merely separated from the blood, dried, and estimated in this condition like the other organic principles.

"The blood furnished by a venesection is whipped on its discharge from the vein according to the process of M. Dumas. The fibrin separates and adheres to the little broom-corns (*brins de balai*). The liquid is passed through a fine cloth to separate that portion of the fibrin which does not adhere to the broom. This fibrin is then washed in a current of water, then dried in a water-bath, and weighed, after having been treated, if desired, with ether to remove a little fatty matter.

"In taking the total weight of the blood which has given this quantity of fibrin, we will have the proportion of the fibrin to the other elements of blood.

"We then take 80 or 90 grammes only of the defibrinated blood which we treat with about twice its volume of a solution of sulphate of soda marking sixteen to eighteen degrees in the aërometer of Baumé, and this is thrown on a half filter weighed in advance, and previously moistened with the saline solution; with these precautions the serum filters quite rapidly with a yellowish colour.

"We understand that, to remove from the globules that remain on the filter, the solution of sulphate of soda with which they are impregnated, we cannot simply wash the filter, for that would dissolve a portion of the globules and the fluid would pass red like the blood. But a property peculiar to the globules allows us, happily, to surmount this difficulty. When they are heated to 90° (Cent.), as Berzelius has already seen, the globules are coagulated entire, and the entire mass becomes concrete without yielding to the water any of the organic matter. We have only, then, to place the filter in a capsule containing boiling water, repeating this process two or three times. The sulphate of soda is dissolved and the water takes almost nothing from the globules, for the fluid is almost colourless and does not contain any organic matter appreciable by tannin or corrosive sublimate.

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[1] Sur une méthode nouvelle pour l'analyse de sang, et sur le constitution chimique des globules sanguins. Par M. L. Figuier. (*Ann. de Chim. et de Phys.*, 1844, 3^{me} série, tome xi. p. 506.)

"To separate the albumen from the filtered serum it suffices to carry it to the point of ebullition in a capsule. The albumen coagulates; it is collected in a little net of fine cloth; it is washed and weighed, after having been dried, by the water-bath. Finally, to determine the quantity of water contained in the blood, we take twenty or twenty-five grammes which we evaporate to dryness in a water-bath. The weight of the residue indicates the properties of water and solid elements.

"The soluble salts of the serum are represented by the difference of the weight of the blood employed and the sum of the albumen, water, fibrin, and globules determined directly."

The above is a very simple and accurate process for determining the globules and organic elements of the blood, but, according to the view we have already taken, is open to the same objection as the other, as it gives the quantity of these ingredients dried, and not as they really exist.

Schmidt, of Dorpat, recognizing the necessity of a proper estimate of the *moist* globules, endeavoured to establish a certain proportion of water to be constantly attributed to them; so that by adding this quantity to the estimate of the dry globules by Provost and Dumas, and others, their results could be made use of. He endeavoured to do this by comparative microscopic measurements of the moist and dry globules, and arrived at the conclusion that the dry globules multiplied by four would give the quantity of moist globules. Though this process was adopted by Lehmann as the most accurate, it is evident that it cannot possibly be exact; especially if the proportion of water in the globules is not always the same, as is stated by Zimmermann.

Zimmermann attempted to give the proportion of water in the globules by estimating the quantity of chlorides in the blood; assuming, with Berzelius, that all the chlorides are contained in the serum and there exist none in the blood. He estimates first the proportion of the chlorides in the serum, then the quantity of chlorides in a given quantity of blood, whence he deduces the proportion of serum in the blood; then subtracting the water contained in the serum from the water contained in the entire blood, he obtains the proportion of water in the globules. As it is by no means certain that the blood-globules contain none of the chlorides, this process cannot be accepted.

Other methods, of a very complicated character, have been proposed by Vierordt, Le Canu, and Lehmann, which it is not necessary to describe, as they present no advantages over the foregoing.

The most recent process which has been proposed originated with Denis, and was published by him in 1859.[1] His manipulations to get rid of the interstitial serum of the globules are complicated and difficult, and of questionable efficacy. He arrives, by this process, at very nearly the results I have obtained by the process of Figuier, which, from its simplicity, is much to be preferred.

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[1] Denis, op. cit.

From this slight review of the processes for the analysis of the blood, especially with reference to the fibrin, albumen, and globules, it is seen that no analysis has ever been made, or even attempted, which would give the real quantities of fibrin and albumen; in all of them the dry residue, and not the substance itself, is given. In the estimation of the globules, however, this desiccating process is so evidently faulty, that efforts have been made to estimate them in their moist state, or as they really exist. As yet there is no one process, for arriving at this end, which is generally accepted by physiological chemists. From my own observations, with regard to all the constituents under consideration, it seems impossible to make an analysis which shall be perfectly accurate; but absolute accuracy is not indispensable; we can get near enough to the truth for all practical purposes, and, as the comparison of different analyses made in the same way gives them much of their value, we should fix upon that process for our estimation of the moist globules which is simplest, and which seems to give the best results. It is manifestly better to get an approximative idea of the fibrin, albumen, and globules of the blood in the condition in which they really exist, than to take the quantity of dry residue, which gives us no idea whatsoever.

Having in view, then, the condition of existence and functions of the organic constituents of the blood, it is only an estimate of these principles in a moist state that can give us any idea of their proportions.

Analytical Process.—In the process which I shall describe, I have endeavoured to simplify manipulations as far as is consistent with tolerable accuracy, deeming it important to put such investigations within the reach of every one, rather than complicate the process by precautions which are designed to avoid errors so slight that they may practically be disregarded. Dumas has shown that the composition of the blood is not precisely the same at the beginning and the end of a bleeding, and recommends, therefore, that the blood be drawn in equal quantities in four vessels, defibrinating the specimens in the second and third, and allowing those in the first and fourth to separate into clot and serum. By comparing the results of the separate analyses, a correction may be made. I have not found it necessary to use more than two specimens of two to four ounces each; and with this quantity such a precaution is not necessary.

It is very important to cover the vessels which contain the blood, and weigh them as soon as possible; for the specimens lose weight very rapidly by evaporation, as has been shown by Becquerel and Rodier,[1] which would interfere seriously with the quantitative analysis.

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[1] In experiments by Becquerel and Rodier with reference to the loss of weight

The blood to be analyzed is taken from the arm, and received into two carefully weighed vessels. The quantity in each vessel may be from two to four ounces. One of the specimens is now whipped with a small bundle of broom-corn, previously moistened and weighed, so as to collect the fibrin; and after the fibrin is completely coagulated, the whole is carefully weighed, deducting the weights of the vessel and broom-corn, which gives the weight of the specimen of blood used. The other specimen is set aside to coagulate.

The first specimen is to be used for the estimation of the fibrin and globules; and the second is set aside to coagulate, and is used to estimate the albumen.

We now pass the first specimen of blood through a fine sieve to collect any fibrin that may not have become attached to the wisp, strip the fibrin from the wisp, and wash it under a stream of water. This may be done very rapidly if we cause the water to flow through a small strainer, so as to break it up into a number of little streams, and knead the fibrin in the fingers, doing this over a sieve so as to catch any particles that may become detached. In this way it may be freed from the globules in five or ten minutes. The fibrin thus washed is then freed from adherent moisture by bibulous paper, and weighed as soon as possible; and by the following simple formula we estimate the proportion per 1000 parts of blood:—

Weight of blood used : Weight of fibrin :: 1000 : Fibrin per 1000.

The next step is to estimate the globules. For this purpose a portion of the defibrinated blood, which is carefully weighed, is mixed with twice its volume of a saturated solution of sulphate of soda, and thrown upon a filter which has been carefully weighed, moistened with distilled water, and just before receiving the mixture of blood and the sulphate of soda, is moistened with the saline solution. The fluid which passes through should be about the colour of the serum; if a few globules pass at first the fluid should be poured back until it is clear. The funnel is then covered and the fluid allowed to separate, the blood-globules being retained on the filter. The filter and funnel are then plunged several times in a vessel of boiling water, by which all the sulphate of soda which remains is washed out, and the blood-globules are coagulated without changing their weight. The funnel should be covered again, and the water allowed to drip from the filter, after which it is weighed, deducting the weight of the

by evaporation, the following results were obtained. The blood was drawn into a porcelain vessel about two and a half inches in diameter:—

	Weight of blood on being drawn from the vein.	Weight of blood 2 hours after.	Weight of blood 24 hours after.
1st Exp. . .	13.242 grammes	13.070 grammes	11.510 grammes
2d Exp. . .	14.905 "	14.727 "	12.977 "
3d Exp. . .	22.453 "	22.308 "	20.337 "

—*Chimie Pathologique*, page 31.

moist filter previously obtained, which gives us the weight of the globules. We obtain the proportion of globules to 1000 parts of blood by the following formula:—

Defibrinated blood used : Globules :: Defibrinated blood per 1000 : Globules per 1000.

Our next step is to estimate the quantity of albumen in the serum, and thence its proportion in the blood. For this purpose we first ascertain the quantity of serum in 1000 parts of blood, which we do by subtracting the sum of the fibrin and globules per 1000 from 1000. Having done this, and waited ten or twelve hours for specimen No. 2 to separate completely into clot and serum, we take a small quantity of the serum, about half an ounce, carefully weigh it, and add suddenly twice its volume of absolute alcohol. The albumen is thus thrown down in a grumous mass, and the whole is thrown on a filter previously moisted with alcohol and weighed. The funnel is immediately covered, and the fluid separates from the albumen very rapidly. We ascertain that no fluid albumen passes through the filter by testing the fluid with nitric acid. After the filter has ceased to drip, it is weighed, and the weight of albumen ascertained by deducting the weight of the filter. The proportion of albumen to 1000 parts of blood is obtained by the following formula:—

Serum used : Albumen :: Serum per 1000 : Albumen per 1000.

The above process is very simple and easy of application, and if the directions be carefully followed, will give very uniform results. I have repeatedly satisfied myself of this fact by subjecting two specimens of the same blood to the same process, which was followed by almost identical, and in some instances, identical results. For example, in an examination of human blood, two equal quantities (34.20 grammes) of defibrinated blood were analyzed for globules; one specimen gave 16.40 grammes of globules, and the other 16.43 grammes. This part of the process would seem more open to the charge of inaccuracy than any, yet the difference in the results of the two analyses is so slight that it may be disregarded.

In washing the fibrin I was at first led to use a saline solution instead of pure water; but as the mass evidently gained weight treated in this way, I afterwards employed simple water. Of two specimens of fibrin from the same blood, one, which was washed with a solution of common salt, spec. grav. 1010, gave 10.28 parts per 1000, and the other, which was washed with water, gave but 8.82 parts, a diminution of about 14 per cent.

I tried most of the methods for coagulating the albumen before fixing upon the one by absolute alcohol. The object was to get it as near as possible in its natural condition, simply changing its form from fluid to semi-solid, without adding anything which would decompose it or unite with it; and absolute alcohol seemed better than heat, nitric acid, the galvanic current, or any of the agents by which it is coagulated. It is necessary to add about twice the volume of alcohol, and suddenly, when the fluid which separates by filtration will be found to contain not a trace of albumen. Repeated trials of different specimens of the same serum, producing generally identical results, led me to fix upon this as the best method.

It is easy to see, after a few trials, why the moist method of estimation of these organic matters has not been employed by chemists. The difficulty is to fix the standard of moisture; for the specimens, even when on the balance, lose weight by evaporation every moment. This, of course, shocks the ideas of accuracy which are necessarily ingrafted into the character of every good analytical chemist. One who is accustomed to weigh for hours, perhaps, to avoid a possible error of the thousandth of a gramme, could not consent to accept a weight which is changing every moment. Perfect desiccation is the only absolutely definite standard; and in all these organic animal analyses, the substance is weighed, and exposed to heat, over and over again, till it ceases to lose weight. Though this accuracy is indispensable in some processes in physiological chemistry, here it is not only unnecessary, but impossible. It is part of the nature of these substances to change every moment, and when they are reduced to such a condition that they will no longer change, they have lost all their characteristics as organic principles. What we want is an approximate physiological idea of their real quantity; and this is better than the most accurate estimate of their dry residue.

By the process just described, I have arrived at the following results in the few quantitative analyses of the blood for organic principles which I have been enabled to make. The variations in these constituents in different states of the human system, and in different animals, are interesting and important; but this demands time and a long series of investigations. In the few observations herein presented, it has been my object to show the advantages of the analytical process employed, so that it can be applied by others, and to give merely an analysis of the healthy human blood; and the various experiments have been made rather to be able to fix upon a definite process, than with a view to comparative results. Attention has been directed only to fibrin, albumen, and globules, for reasons which have already been fully explained. As far as the other constituents are concerned, I have not the temerity to suppose that I could improve upon the processes employed by the eminent hematologists to whom I have so often referred in this paper. The number of analyses of human blood is not large, for it is not easy to obtain healthy specimens; and with our improved notions of therapeutics, it is difficult also to obtain specimens of blood from patients. The specimens of human blood were taken from the arm. The blood of the ox was taken in the slaughter house, the vessels of the neck being divided after the animal had been knocked on the head.

Examination I. *Human Blood, Male.*—This specimen of blood is assumed to be perfectly normal. The subject was 27 years of age, male, perfectly healthy, and had never suffered from disease. Weight, 170 pounds. The blood was taken from the arm at 1 P. M. The last meal had been taken at 8 A. M.

The following is the result of analysis of the blood:—

Fibrin	8.82	parts	per 1000.
Albumen	329.82	"	"
Globules	495.59	"	"

Examination II. *Human Blood, Male.*—This specimen was taken from a man, 37 years of age, calker by trade, weight 200 pounds, but rather corpulent than muscular. He had slight constitutional syphilis, and had been taking the iodide of potassium, gr. x three times a day, for about three weeks. He was bled from the radial vein about two hours after dinner.

The following is the result of analysis of the blood:—

Fibrin	7.44	parts	per 1000.
Albumen	277.55	"	"
Globules	480.44	"	"

Examination III. *Human Blood, Female.*—This specimen was taken from a female, 27 years of age, weight 160 pounds, dark complexion, and perfectly healthy, with the exception of a slight plethoric tendency, as indicated by occasional epistaxis which had troubled her for a few days. She menstruated regularly, the last time about two weeks before. She took lunch about 11 A. M., and was bled at 2 P. M. The blood coagulated rapidly, and in twelve hours the clot presented the "buffed and cupped" appearance in a marked degree. A portion of the defibrinated blood which was not used in the analysis presented a remarkable example of gravitation of the globules and separation from the serum. It stood in a graduated glass, and the upper half, by measurement, consisted of pure serum. The whole fluid was f℥xii⅔, and the globules marked f℥vi⅓.[1] Two days after the venesection the woman still enjoyed perfect health.

The following is the result of analysis of the blood:—

Fibrin	16.81	parts	per 1000.
Albumen	311.18	"	"
Globules	484.51	"	"

Examination IV. *Human Blood, Female.*—This specimen was taken from a woman, 28 years of age, of somewhat anæmic aspect. She had been taking ℥j of sulphate of magnesia every second day for two weeks.

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[1] This tendency of the globules to gravitate in defibrinated blood was noticed by Poiseuille, and is mentioned by Bernard, who advances the view that one of the important functions of fibrin is to keep the globules in uniform suspension. (Bernard, *Liquides de l'Organisme*, tome i. p. 465.) The phenomenon is by no means invariable. I have seen specimens of blood in which there was no gravitation of the globules. Such a complete separation as was presented in this specimen of blood is very remarkable.

The medicine usually operated three or four times. She was bled at 2 P. M., having eaten nothing since 8 A. M.

The following is the result of analysis of the blood:—

Fibrin	11.34 parts per 1000.
Albumen	219.47 " "
Globules	382.95 " "

Examination V. *Blood of the Ox.*—This specimen was taken from a small ox, the throat being cut after he had been knocked in the head.

The following is the result of the analysis:—

Fibrin	14.52 parts per 1000.
Albumen	195.24 " "
Globules	623.36 " "

Examination VI. *Blood of the Ox.*—The animal from which this specimen was taken was rather larger and more vigorous than the one which furnished the blood in Exam. V.

The following is the result of the analysis:—

Fibrin	16.27 parts per 1000.
Albumen	200.85 " "
Globules	568.61 " "

Of the four observations on the human subject, but one, Exam. I., can be taken as a fair example of normal blood. This analysis shows that the moist globules constitute about one-half of the entire mass of blood; an estimate which does not differ very considerably from the results obtained by others who have endeavoured to solve this question. Denis gives the proportion of globules in a person "30 years of age, strong constitution, sanguine temperament," 489.52 parts per 1000.[1] Schmidt estimates the moist globules at 513 per 1000 for the male and 396 for the female.[2] Lehmann estimates them at 496 per 1000.[3]

The albumen constitutes by far the greater part of the other organic matter, and forms nearly one-third of the entire weight of blood. As this is undoubtedly the element which nourishes the organic parts of the tissues, which form the greater part of the body, we are not surprised at its preponderance. The fibrin we see, even by this mode of analysis, exists in small quantity; sufficient, however, to firmly coagulate the whole mass of blood. One is surprised in washing a large clot to see how little fibrin is necessary to thus entangle all the globules. The salts were found to exist in the fibrin, albumen, and globules, which were all tested for chlorides, carbonates, phosphates, and sulphates.

Taking Becquerel and Rodier as authority for the proportion of fatty, inorganic, and extractive matter, the following table represents the composition of the blood in a healthy adult male.

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[1] Denis, Mémoire sur le Sang., Paris, 1859, p. 427.

[2] Milne Edwards, Leçons de Physiologie, &c., tom. i. p. 237.

[3] Lehmann, Physiological Chemistry, American edition, vol. i. p. 548.

COMPOSITION OF THE BLOOD.[1]

	Globules	495.59
Plasma.	Water	155.42
	Fibrin	8.82
	Albumen	329.82
	Fats, inorganic salts, and extractives (B. & R.)	10.35
		1,000.00

We have not yet sufficient data to arrive at any definite conclusions with regard to the variations of the organic constituents of the blood, as regards sex, conditions of the system, and in different animals, which, indeed, would be beyond the scope of this paper; but the few facts we have collected go to confirm some of the observations which have already been made upon these points. It has been often observed that the blood of the ox is much richer in fibrin than that of the human subject, the former containing from 5 to 6 parts per 1000 dry, while the latter contains but from 2 to 3. This difference is shown in the preceding analysis, where the blood of the ox is found to contain 14.52 to 16.27 parts of moist fibrin, human blood containing but 8.82 parts. The analysis also shows a greater quantity of fibrin in the two specimens of blood of the female than in the blood of the male. In the observations of others the quantity has not been found to vary much in the sexes. In this instance neither of the specimens from the female could be taken as perfectly normal; as in Examination III. the subject was plethoric, and in Examination IV. she had been taking sulphate of magnesia, and was somewhat anæmic.

The albumen was found to vary considerably in the specimens of human blood, being more abundant in the blood of the male in Examination I. than the female in Examination III. and IV., but less in the blood of the male in Examination II. than in the female in Examination III. There are not here sufficient data to form any conclusion with regard to the variations of albumen in the sexes. In the blood of the ox, the albumen was much less than in human blood.

The quantity of globules was found to be greater in the male than in the female. This has been noticed by all observers who have directed their

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[1] In order to ascertain whether this specimen of blood contained what would be considered the normal quantity of organic constituents estimated by the old method, these were evaporated to dryness and weighed carefully, with the following result, which it will be seen corresponds with that generally obtained:—

Fibrin	2.50	parts per 1000.
Albumen	71.53	" "
Globules	125.00	" "

The proportion of albumen to the serum was 82.07.

attention to this subject, and is, perhaps, one of the most characteristic differences between the blood of the male and of the female. One of the females was slightly plethoric, which caused the globules to mount up nearly to the standard of the healthy male. This condition of plethora, according to Andral, is dependent almost entirely upon an increase in the globules. The difference in this respect between the blood of the female who was slightly plethoric, and the other, who was somewhat anæmic, is very marked; in the former the globules are 484.51 and in the latter 382.95. The blood of the ox was found to be very rich in globules.

In conclusion, I beg leave to state that I have not attempted in this paper to settle the normal constitution of the blood, much less to follow out the variations to which it is subject. This would require a largely extended series of observation. But, considering a proper idea of the condition of existence of the organic ingredients of immense importance to the physiologist and physician, I have endeavoured to study this fluid from a physiological point of view; and, with the ideas I have been led to entertain on this subject, it seemed that a new mode of analysis was indispensable, which would give us the real proportions of these principles. My object has been merely to settle upon some rational and simple process, leaving its extended applications to be made in the future. The process I have described seems to me sufficiently accurate for all practical purposes; and is so easy of application, that I cannot but indulge the hope that many may be led to cultivate this interesting and fruitful field of inquiry.

Art. V.—*Conservative Medicine as Applied to Hygiene.* By Austin Flint, M. D., Professor of the Principles and Practice of Medicine in the Bellevue Hospital Medical College, and in the Long Island College Hospital.

As the phrase *Conservative Medicine* may be misconstrued, a brief explanation is to be premised. The term Conservatism may be used to express a principle which leads the practitioner, in dealing with diseases, to preserve, develop, and support the vital powers. The unfolding of this principle more and more during the last quarter of a century, has been a result of the progressive increase of the knowledge of the organism in health and disease, together with the accumulating fruits of clinical experience; it is the characteristic of the therapeutics of the present time, as represented by the views of the ablest writers and practitioners, and it is claimed that it should be considered as the governing principle in medical practice. For a fuller exposition, the reader is referred to the previous articles on the subject.[1]

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[1] *Vide* Am. Journ. of Med. Sciences, No. for January, 1863.